

Practitioner's Docket No. 2245/109

CHAPTER II

Preliminary Classification:

Proposed Class:

Subclass:

TRANSMITTAL LETTER  
TO THE UNITED STATES ELECTED OFFICE (EO/US)

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

PCT/GB00/03892	11 October 2000 (11.10.00)	11 October 1999 (11.10.99)
International Application Number	International Filing Date	International Earliest Priority Date

TITLE OF INVENTION: Medicament Delivery Device with Moisture Resistant Coating

APPLICANT(S): Braithwaite, Philip

Box PCT  
Commissioner for Patents  
Washington D.C. 20231  
ATTENTION: EO/US

CERTIFICATION UNDER 37 C.F.R. SECTION 1.10\*

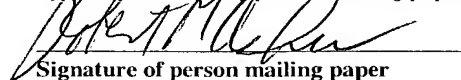
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I hereby certify that this paper, along with any document referred to, is being deposited with the United States Postal Service on this date 21 March 2002, in an envelope as "Express Mail Post Office to Addressee," mailing Label Number EL 603053865 US, addressed to the: Commissioner for Patents, Washington, D.C. 20231, Box PCT, Attn: EO/US.

Robert M. Asher

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WARNING

Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. Section 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.

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"Since the filing of correspondence under [Section] 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will not be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442

10/088843

JC10 Rec'd PCT/PTO 21 MAR 2002

1. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. Section 371:

- a. This express request to immediately begin national examination procedures (35 U.S.C. Section 371(f)).
- b. The U.S. National Fee (35 U.S.C. Section 371(c)(1)) and other fees (37 C.F.R. Section 1.492) as indicated below:

2. Fees

CLAIMS FEE*	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
BASIC FEE	TOTAL CLAIMS	21 -20 =	1	x \$18.00 =	\$18.00
	INDEPENDENT CLAIMS	2 -3 =	0	x \$84.00 =	\$0.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable) + \$280.00				\$0.00
	U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in Section 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in Section 1.445(a)(2) to the U.S. PTO: where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 C.F.R. Section 1.492(a)(5)) ..... \$890.00				\$890.00
	Total of above Calculations				= \$908.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed (note 37 CFR Sections 1.9, 1.27, 1.28)				- \$0.00
	Subtotal				\$908.00
	Total National Fee				\$908.00
	Fee for recording the enclosed assignment document \$40.00 (37 C.F.R. Section 1.21(h)) See attached "ASSIGNMENT COVER SHEET".				\$0.00
TOTAL	Total Fees enclosed				\$908.00

A check in the amount of \$908.00 to cover the above fees is enclosed.

3. A copy of the International application as filed (35 U.S.C. Section 371(c)(2)) has been transmitted by the International Bureau.

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4. A translation of the International application into the English language (35 U.S.C. Section 371(c)(2)) is not required as the application was filed in English.
5. Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. Section 371(c)(3)) have been transmitted by applicant on 1 October 2001.
6. A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. Section 371(c)(3)) has not been transmitted for reasons indicated in section 5.
7. A copy of the international examination report (PCT/IPEA/409) is transmitted herewith.
8. Annex(es) to the international preliminary examination report is/are transmitted herewith.
9. A translation of the annexes to the international preliminary examination report is not required as the annexes are in the English language.
10. An oath or declaration of the inventor (35 U.S.C. Section 371(c)(4)) complying with 35 U.S.C. Section 115 will follow.

II. Other document(s) or information included:

11. An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a) is transmitted herewith.
12. An Information Disclosure Statement under 37 C.F.R. Sections 1.97 and 1.98 will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. Section 371(c).
13. Additional documents:
  - a. International Publication No. WO01/27210  
Specification, claims and drawing
14. The above items are being transmitted before 30 months from any claimed priority date.

**AUTHORIZATION TO CHARGE ADDITIONAL FEES**

The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No.: 19-4972

37 C.F.R. Section 1.492(a)(1), (2), (3), and (4) (filing fees)

37 C.F.R. Section 1.492(b), (c), and (d) (presentation of extra claims)

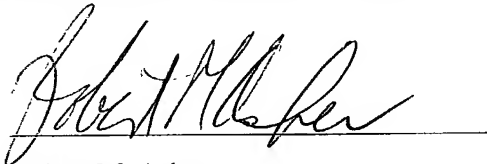
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37 C.F.R. Section 1.17 (application processing fees)

37 C.F.R. Section 1.17(a)(1)-(5) (extension fees pursuant to Section 1.136(a))

Date: 21 March 2002



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Title Line One:: Medicament Delivery Device with Moisture  
Title Line Two:: Resistant Coating  
Application Type:: Utility  
Docket Number:: 2245/109

Representative Customer Number:: 2101

This application is a:: 371 of  
> Application One:: PCT/GB00/03892  
Filing Date:: 11 October 2000

Foreign Application One:: 9923959.2  
Filing Date:: 11 October 1999  
Country:: GB  
Priority Claimed:: Yes

Foreign Application Two:: 0017314.6  
Filing Date:: 15 July 2000  
Country:: GB  
Priority Claimed:: Yes

MEDICAMENT DELIVERY DEVICE WITH MOISTURE RESISTANT COATING

This invention relates to a novel form of reservoir means, such as a medicament capsule and the like and to a delivery device e.g. an inhaler, for use in administering a medicament in such a reservoir means.

Many medicament delivery devices, such as inhalers, make use of medicament in a finely divided powder form. The powder may be located within the delivery device, for instance, in a single storage compartment or in a plurality of single dose locations.

One form of inhaler may make use of medicament powder which is located within a frangible, plastic capsule. In use, the capsule is inserted into the inhaler and operation of the inhaler ruptures from the plastic capsule so that the powder may be extracted from the capsule and inhaled by the user.

A problem encountered with many such devices making use of powdered medicament is that, if moisture comes into contact with the powder, it will tend to make it less free-flowing and therefore render the operation of the device less effective because the correct dose of powder cannot be fully delivered.

Moisture may access the powder via several different mechanisms. These include the passage of the moisture through, for example, the plastic wall of encapsulated powder for those inhalers which make use of capsules loaded with medicament powder. For those inhalers which include a storage compartment loaded with powder and from which a dose of powder is accessed by some form of moving part within the inhaler and then presented to an air passageway for inhalation, moisture can access powder within the storage compartment by finding its way along a gap or gaps between the moving parts. In some inhalers there is the possibility of a "wick" type path being established between the powder in a storage compartment within the inhaler and a location within the inhaler where a dose of medicament is located.

With inhalers where a plurality of single doses of medicament is located within the inhaler, there is again likely to be one or more moving parts, providing gaps along which moisture may travel to access each individual dose of medicament.

- 5 It is also possible that moisture can pass through the plastic walls of inhalers and reach the powder contained within the inhaler whether in a single storage compartment or in individual dosage locations.

10 International Patent Application No WO 00/12163 describes the use of a Parylene coating on the inner surface of the metering chamber which is intended to mitigate the deposition of medicament particles on the inner walls of a metered dose inhaler (MDI) for the delivery of medicament via a pressurised aerosol.

15 We have now surprisingly found that a moisture resistant coating, e.g. a Parylene coating, may be used as on a medicament reservoir and/or a medicament delivery device, such as an inhaler, to render the device, and especially the medicament chamber, moisture resistant.

20 According to a first aspect of the invention we provide a reservoir means which means is provided with a moisture resistant coating.

In a preferred embodiment, the reservoir means contains medicament such that the reservoir means may be used in conjunction with a delivery device.

25 The reservoir means may be any conventionally known reservoir means, such as a bulk medicament reservoir or one or more single dose reservoir means. The reservoir means shall not include a pressurised canister for use in inhalation therapy as described in the prior art. When the reservoir means is a single dose reservoir, such as a capsule, e.g. a conventional gelatin capsule, or a spool and spool carrier as  
30 described in International Patent Application No. WO93/16748, the coating may be on the inner walls or the outer walls of the reservoir means. However, preferably, the

reservoir means is coated on the outer walls, such that the reservoir means is substantially sealed in the coating and is rendered moisture proof. The medicament reservoir may comprise a plurality of single dose units housed in a cartridge. In such a case, the cartridge may also be provided with a moisture resistant coating.

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According to a further feature of the present invention we provide a medicament delivery device which comprises a medicament reservoir as hereinbefore described.

In an especially preferred embodiment the medicament delivery device is also provided with a moisture resistant coating. Such a coating preferentially covers substantially the whole of the delivery device.

When the medicament reservoir means comprises a bulk reservoir, then the medicament delivery device may preferentially include a metering member. The metering member preferably is also provided with a moisture resistant coating.

According to a yet further feature of the invention we therefore provide a medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member characterised in that the device is provided with a moisture resistant coating on one or more surfaces. Preferably, the whole of the device is substantially provided with a moisture resistant coating.

The moisture resistant coating may be provided on one or more external or internal surfaces of the body of the medicament delivery device. The moisture resistant coating preferentially coats one or more surfaces of the bulk medicament reservoir. Other surfaces of the body of the medicament delivery device may also be provided with a moisture resistant coating.

The moisture resistant coating may be in the form of any material which is effective to prevent moisture accessing the powder. Typically, it may be applied to those surfaces between which there may be a gap due to relative movement between the

surfaces when the inhaler is in use. However, the moisture resistant coating may be applied additionally or alternatively to other surfaces including the whole or part of

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the external surface of the inhaler in order to prevent moisture passing into the interior of the inhaler through the walls thereof.

5 The moisture resistant coating should, of course, be sufficiently stable and robust so that damage to the coating during use of the delivery device.

The moisture resistant coating of the invention may be applied to any conventionally known medicament delivery system. However, in a preferred embodiment, the medicament delivery device is an inhaler. Whilst the moisture proof barrier may be  
10 applied to any conventionally known inhaler, it is an especially preferred aspect of the invention for the inhaler to be a dry powder inhaler (DPI).

Thus, in a preferred embodiment we provide an inhaler, e.g. a DPI, in which the medicament reservoir is provided with a moisture resistant coating.

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Dry powder inhalers are known, such as TECHNOHALER, being developed by Innovata Biomed in the UK. WO 93/16748 describes an inhaler which comprises a disc-like cartridge having a plurality of medicament carrying capsules around its periphery. Each capsule comprises a spool carrier which houses a spool. Each spool  
20 has a flange at each end which form a tight slidable fit within the body of the spool carrier. The space left between the body of the spool and the spool carrier is filled with an appropriate medicament.

In a preferred embodiment we provide a dry powder inhaler wherein the medicament  
25 reservoir comprises one or more individual medicament capsules, e.g. spool carriers and wherein each medicament capsule is provided with a moisture resistant coating. Preferably, the medicament capsule is sealed in a moisture resistant coating.

A variety of medicaments may be administered by using the inhaler of the invention.  
30 Such medicaments are generally (but not limiting), bronchodilators or other anti-asthma drugs or antibiotics. Such medicaments include, but are not limited to  $\beta_2$ -

agonists, e.g. fenoterol, formoterol, pirbuterol, reproterol, rimiterol, salbutamol, salmeterol and terbutaline; non-selective beta-stimulants such as isoprenaline; xanthine bronchodilators, e.g. theophylline, aminophylline and choline theophyllinate; anticholinergics, e.g. ipratropium bromide; mast cell stabilisers, e.g. sodium cromoglycate and ketotifen; bronchial anti-inflammatory agents, e.g. nedocromil sodium; and steroids, e.g. beclomethasone dipropionate, fluticasone, budesonide and flunisolide; and combinations thereof.

Specific combinations of medicaments which may be mentioned include combinations of steroids, such as, beclomethasone dipropionate, fluticasone, budesonide and flunisolide; and combinations of to  $\beta_2$ -agonists, such as, formoterol and salmeterol. It is also within the scope of this invention to include combinations of one or more of the aforementioned steroids with one or more of the aforementioned  $\beta_2$ -agonists.

Further medicaments may include proteinaceous compounds and/or macromolecules, for example, leuprolide and alpha interferon; hormones, such as insulin, human growth hormone, parathyroid hormone; growth factors, anticoagulants, immunomodulators, cytokines and nucleic acids.

According to a yet further feature of the invention we provide a method of treating a respiratory disorder which comprises the administering of a therapeutically effective amount of a pharmaceutically active agent to a patient suffering from such a disorder.

The moisture resistant coating is preferentially a biocompatible coating. Such coatings include, but are not limited to, sugars.

Polymers of poly-para-xylylenes are known as parylene. This material is a conformal polymer film which has been used in a number of applications, including electronics circuits and sensor, where environmental and dielectric isolation is required.

We further the use of a parylene in the manufacture of a moisture resistant capsule as hereinbefore described.

Parylenes are thermoplastic polymers that are capable of polymerising on surfaces  
 5 from an active monomer gas, without the presence of a liquid. The process is capable of producing very thin layers of polymer and, indeed, a layer of from 10 to 20 microns may be sufficient to protect inhalers and their parts from ingress of moisture.

The polymerisation process takes place at room temperature without solvents and  
 10 additives. Since the parylene is applied as a gas it conforms to the topography of the surface which it contacts. Since the process does not involve a liquid phase, there is no pooling and bridging during application. The coating is free of pinholes even if the coating has a thickness of less than one micron. As well as being resistant against moisture, parylene is also resistant against other media including hydrocarbons, acids  
 15 and blood.

The coating may be applied in a single vacuum-coating operation in a thickness from 0.025 to 75 microns and can be controlled accurately to  $\pm 10\%$  of the final thickness.

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## CLAIMS

1. An inhaler which includes a medicament reservoir means which means is provided with a moisture resistant coating characterised in that the reservoir means is coated on the outer walls, such that the reservoir means is substantially sealed in the coating and is rendered moisture proof.  
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2. An inhaler means according to claim 1 characterised in that the reservoir means contains a medicament.  
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3. An inhaler means according to claim 1 characterised in that the reservoir means is a bulk medicament reservoir.
4. An inhaler means according to claim 1 characterised in that the reservoir means comprises one or more single dose reservoir means.  
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5. An inhaler according to claim 1 characterised in that the reservoir means comprises a spool carrier housing a spool.
- 20 6. An inhaler means according to claim 1 characterised in that the moisture resistant coating is a biocompatible coating.
7. An inhaler means according to claim 6 characterised in that the biocompatible coating is a sugar.  
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8. An inhaler means according to claim 6 characterised in that the moisture resistant coating is a polymer.
9. An inhaler means according to claim 8 characterised in that the polymer is a poly-para-xylylene (parylene).  
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20. The use of a parylene in the manufacture of an inhaler according to claim 1.

21. An inhaler substantially as described with reference to the accompanying  
5 description.

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P36234WO.1 amended claims

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
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PCT

(10) International Publication Number  
**WO 01/27210 A1**

- (51) International Patent Classification<sup>7</sup>: C09D 165/04, B65D 83/14 (74) Agent: HARRISON GODDARD FOOTE; Tower House, Merrion Way, Leeds LS2 8PA (GB).
- (21) International Application Number: PCT/GB00/03892 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
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9923959.2 11 October 1999 (11.10.1999) GB  
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- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
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- Published:  
— With international search report.
- (72) Inventor; and
- (75) Inventor/Applicant (*for US only*): BRAITHWAITE, Philip [GB/GB]; ML Laboratories Plc, 13 Alexandra Way, Ashchurch Industrial Estate, Tewkesbury GL20 8NB (GB).
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MEDICAMENT DELIVERY DEVICE WITH MOISTURE RESISTANT COATING

(57) Abstract: There is described a reservoir means which means is provided with a moisture resistant coating, the reservoir means is especially adapted to contain a medicament. There is also described a medicament delivery device which comprises a medicament reservoir, a medicament delivery passage and a metering member characterised in that the device includes a surface or surfaces provided with a moisture resistant coating. The device is especially an inhaler, e.g. a dry powder inhaler. A method of treating a respiratory disorder is also described which comprises administering of a therapeutically effective amount of a pharmaceutically active agent to a patient suffering from such a disorder.

WO 01/27210 A1

Practitioner's Docket No. 2245/109

*PATENT*

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**COMBINED DECLARATION AND POWER OF ATTORNEY**

**(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL,  
CONTINUATION, OR C-I-P)**

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As a below named inventor, I hereby declare that:

**TYPE OF DECLARATION**

This declaration is for a national stage of PCT application.

**INVENTORSHIP IDENTIFICATION**

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am the original, first and sole inventor of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

**TITLE OF INVENTION**

Medicament Delivery Device with Moisture Resistant Coating

**SPECIFICATION IDENTIFICATION**

The specification was described and claimed in PCT International Application No. PCT/GB00/03892 filed on October 11, 2000 and was amended under PCT Article 19 on October 1, 2001.

**ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR**

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, Section 1.56, and which is material to the examination of this application, namely, information where there is a substantial likelihood that a reasonable Examiner would consider it important in deciding whether to allow the application to issue as a patent.

**ALL FOREIGN APPLICATION(S), IF ANY, FILED MORE THAN 12 MONTHS  
(6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION**

GB 9923959.2  
GB 0017314.6

**POWER OF ATTORNEY**

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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15

I hereby appoint the practitioner(s) associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

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Customer Number 2101

**DECLARATION**

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

**SIGNATURE(S)**Philip Braithwaite

Inventor's signature

Date 21/05/02

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